Media Release
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Phase 2 data of selatogrel, Idorsia's highly-selective P2Y12 receptor antagonist, presented at ESC 2019

- Phase 2 clinical data demonstrated that subcutaneous administration of selatogrel resulted in a potent, rapid and sustained platelet inhibition effect, and was safe and well tolerated
- The company is preparing for a Phase 3 study for the treatment of a suspected acute myocardial infarction

Allschwil, Switzerland – September 3, 2019
Idorsia Ltd (SIX: IDIA) today announced that the positive results of two Phase 2 clinical studies with selatogrel, a highly-selective $P2Y_{12}$ receptor antagonist, were presented at the European Society of Cardiology 2019 Congress in Paris, France. The company is now in the process of preparing for a Phase 3 study to investigate the efficacy and safety of selatogrel following subcutaneous self-administration for the treatment of a suspected acute myocardial infarction (AMI) in adult patients with a history of AMI.

An AMI, or heart attack, is a life-threatening condition that occurs when blood flow to the heart muscle is suddenly decreased or completely cut off. It is usually caused by a blood clot or blockage in one or more of the coronary vessels supplying blood to the heart muscle. An AMI requires immediate treatment and medical attention, as any delay in intervention can result in irreversible damage to the heart muscle. The American Heart Association estimates that each year more than 600,000 persons living in the US will suffer their first heart attack and around 200,000 will suffer a recurring heart attack.

AMI is associated with a 30% mortality rate and about half of these deaths occur prior to arrival at the hospital. As a result, early action is crucial for survival, however there are no treatment options available for the critical time from onset of AMI symptoms to first medical contact. The need for an early intervention has been highlighted by the guidelines of the European Society of Cardiology and the American College of Cardiology / American Heart Association, which identified the prehospital phase as the most critical and reiterated that efforts must be made to reduce the delay for treatment initiation to reduce death.

About selatogrel
Idorsia is developing selatogrel, a potent, fast-acting, reversible, and highly-selective $P2Y_{12}$ receptor antagonist, for single subcutaneous self-administration for the treatment of a suspected AMI in patients with a history of AMI.

Martine Clozel, MD and Chief Scientific Officer, commented:
"It is well documented that AMI is caused by blood vessel occlusion, driven by the formation of a platelet-rich thrombus which can be prevented by $P2Y_{12}$ receptor antagonists. This therapeutic class has been used in the treatment of millions of patients globally and as such, the safety and efficacy profiles are well-established. However, until now the method of administration or the delayed onset of effect means that currently available treatments do not have the desired profile to cover the critical time from onset of AMI symptoms to first medical contact. Scientists at Idorsia have discovered selatogrel, which has great potential to fill this gap for early treatment of AMI."

About the clinical development of selatogrel

Subcutaneous administration of selatogrel by a healthcare professional has been studied in two Phase 2 clinical studies in patients with stable coronary artery disease (CAD) and in patients with AMI, which were both presented at ESC 2019.

Phase 2 study in adults with stable CAD presented at ESC

Professor Robert Storey, BM, Professor of Cardiology, University of Sheffield, UK, gave an oral presentation entitled *"Selatogrel, a novel $P2Y_{12}$ receptor antagonist, achieves rapid, consistent and sustained platelet inhibition following single-dose subcutaneous administration in stable CAD patients"*.

The study was a multicenter, double blind, randomized, placebo-controlled study assessing the pharmacodynamics, pharmacokinetics, tolerability and safety of a single subcutaneous injection of selatogrel either in the thigh or in the abdomen at 2 different doses in adults with stable coronary artery disease. In the study, 345 patients (mean age 65 y; 20% female; 31% diabetes) received selatogrel 8 mg (n=114), selatogrel 16 mg (n=115) or placebo (n=116). 97% were on background therapy with aspirin (or its derivative carbasalate) and 35% on oral $P2Y_{12}$ receptor antagonist (clopidogrel 23%, prasugrel 4%, ticagrelor 8%). The primary objective of the study was to characterize inhibition of platelet aggregation relative to placebo. Platelet reactivity was assessed by VerifyNow PRU ($P2Y_{12}$ reaction units) test before and 15 min, 30 min and 1, 2, 4, 8 and 24 h after injection. Light-transmittance aggregometry (LTA; ADP 20 uM) was also performed.

The primary endpoint, patients (responders) having PRU < 100 starting at 30 min and lasting ≥3 h after a single study treatment injection, was achieved in 89% of patients receiving selatogrel 8 mg, and 90% of patients receiving selatogrel 16 mg compared with 16% in the placebo group (P<0.0001). Inhibition of platelet aggregation was observed as early as 15 min post-dose, PRU values (mean±SD) were 10±25 with selatogrel 8 mg, 5±10 with selatogrel 16 mg and 163±73 with placebo. PRU levels were maintained at 2 and 4 h for both doses and gradually returned to pre-dose levels by 24 h post-dose. Light-transmittance aggregometry (LTA) results were consistent with the VerifyNow results. Pharmacodynamic responses were similar for thigh and abdomen injection sites and were consistent across the different subgroups (age, sex, BMI, presence of chronic kidney disease or diabetes). Selatogrel was well tolerated: mild dyspnea (or moderate dyspnea, n=1, with 16 mg) occurred in 5% and 9% of patients with selatogrel 8 mg and 16 mg, respectively, vs 0% with placebo; dizziness occurred in 4% and 4% vs 1%, respectively, without significant hemodynamic or ECG changes. Bleeding events occurred in 9.6% and 4.3% of patients with selatogrel 8 mg and 16 mg, respectively, vs 6.9% with placebo. All bleeding events were of mild intensity except one of moderate intensity, which was reported in the placebo group. No major bleeding event was reported during the study.

Prof. Robert Storey commented:

"Pivotal trials of anti-platelet drugs in patients with AMI have demonstrated the importance of rapid onset of action yet, more recently, we have learnt that the onset of action of oral anti-platelet drugs may be delayed by hours in this setting. In this context, the properties of selatogrel that we have demonstrated in patients with CAD are particularly exciting and demonstrate the potential for further advancing the early management of AMI by delivering rapid and consistent platelet inhibition with a simple single subcutaneous administration."

Phase 2 study in adults with AMI presented at ESC

Professor Peter Sinnaeve, MD, Department of Cardiology, University Hospitals Leuven, Faculty of Medicine, University of Leuven, Belgium, gave an oral presentation entitled *"Inhibition of platelet aggregation after subcutaneous administration of a single-dose of selatogrel, a novel $P2Y_{12}$ receptor antagonist, in patients with acute myocardial infarction"*.

The study was a multi-center, open-label, randomized, exploratory study to assess the onset of platelet aggregation inhibition after a single subcutaneous injection of selatogrel in adults with acute myocardial infarction. In this study, 47 patients (median age 69 y; 72% male; 62% STEMI; 94% Killip class 1) received 8 mg (n=24) or 16 mg (n=23) selatogrel. Study-treatment concomitant medications included acetylsalicylic acid (98%), $P2Y_{12}$ receptor antagonists (96%), heparins (94%), statins (94%), nitrates (68%) and morphine (38%). Blood samples were collected at baseline and at 15, 30, and 60 min post-dose and platelet reactivity (expressed as PRU) was evaluated using VerifyNow. The primary objective of the study was to assess the inhibition of platelet aggregation 30 minutes after a single subcutaneous injection of selatogrel.

The response to treatment as defined by PRU < 100 at 30 min post-dose, was achieved in 91% and 95% of patients with selatogrel 8 and 16 mg, respectively. Response rates were independent from STEMI/NSTEMI diagnosis, age and sex. PRU below 100 was observed as early as 15 min (8 mg: 75% of patients; 16 mg: 91% of patients) and sustained for up to 60 min post-dose (8 mg: 75% of patients; 16 mg: 96% of patients). Overall, 43% of patients had ≥1 treatment-emergent adverse event (TEAE), which were mainly of mild/moderate intensity. Ventricular tachycardia ([VT] 8 mg: 4/24; 16 mg: 3/23) was the most frequent TEAE and was reported as serious AE in two patients: one patient receiving 8 mg and one patient receiving 16 mg selatogrel. Post-procedural hemorrhage (of mild intensity) occurred in one patient after percutaneous coronary intervention with radial access.

Prof. Peter Sinnaeve commented:
"The concept that "time is muscle" in relation to AMI has been around for nearly 30 years, yet we still don't have anything to offer our patients in the time between onset of AMI symptoms and first medical contact, which can often be several hours. The anti-platelet effect and safety profile observed in this Phase 2 program of selatogrel suggests that it has the potential to overcome limitations of available oral $P2Y_{12}$ receptor antagonist therapies in the early management of AMI. Any reduction in the delay for treatment initiation could mean the difference between life and death, so we must evaluate this opportunity."

Guy Braunstein, MD and Head of Idorsia Global Clinical Development, added:
"The Phase 2 data demonstrate that subcutaneous administration of selatogrel 16mg in patients with stable CAD and patients with AMI has a rapid onset of action, within 15 minutes, with the effect extending over 4-8 hours. Based on the speed at which selatogrel takes effect, the duration of that effect, and the safety and tolerability profile, self-administration of selatogrel at the very onset of symptoms of a suspected AMI has potential as a highly innovative approach to AMI management."

In consultation with health authorities, Idorsia is preparing a large, international, multi-center, Phase 3 study to investigate the efficacy and safety of subcutaneous self-administration of selatogrel for the treatment of a suspected AMI in patients with an history of AMI. Participating patients will be trained on when to inject and instructed on how to self-administer treatment. An integrated drug delivery device is being developed through usability and reliability studies to ensure functional efficacy can be demonstrated ahead of the Phase 3 study.

Jean-Paul Clozel, MD, and Chief Executive Officer, concluded:
"As a cardiologist, I find this project incredibly exciting. I think everyone understands that this novel concept of self-administration at onset of symptoms could be a game-changer in the management of AMI. As a CEO, I am also excited for the impact this product could have on the future of our company. As some of our Phase 3 programs are approaching completion, the timing is perfect to bring new innovative projects forward and deliver on our vision to help more patients."

Notes to the editor

About Professor Robert Storey

Professor Robert Storey is Professor of Cardiology at the University of Sheffield, Sheffield, UK, where he has headed a thrombosis research group since 2002 and is director of the Cardiovascular Research Unit. In addition, Prof. Storey is Academic Director and honorary Consultant Cardiologist for the Cardiology and Cardiothoracic Surgery Directorate, Sheffield Teaching Hospitals NHS Foundation Trust. He has a special interest in the management of ischaemic heart disease, including acute coronary syndromes and coronary intervention.

He was Chair of the Working Group on Thrombosis of the European Society of Cardiology (ESC) from 2012-2014 and has been a Task Force member for ESC guidelines on chronic coronary syndromes (2019), non-ST-elevation acute coronary syndromes (2011 and 2015) and dyslipidaemias (2011). He served as a member of the executive committees for the DISPERSE2, PLATO and PEGASUS-TIMI 54 studies, leading the platelet function substudies for these trials, and of the steering committees for the TRA-CER, EPICOR, ATLANTIC and AUGUSTUS studies. He is currently chief investigator for a phase II study of selatogrel in stable coronary artery disease patients and a member of the steering committees for the COMPLETE, RAPID CTCA, SENIOR RITA and CLEAR SYNERGY studies.

About Professor Peter Sinnaeve

Dr Peter Sinnaeve graduated summa cum laude from the University of Leuven, Belgium, in 1994, and was trained as a cardiologist at the same institution. He subsequently obtained a PhD degree in Medical Sciences, after doctoral research in cardiovascular gene therapy. In 2002-2003, he was a post-doctoral fellow at the Duke Clinical Research Institute in the USA as recipient of a Fullbright scholarship. Dr Sinnaeve then joined the staff at the University Hospitals Leuven, Belgium. He is currently professor at the University of Leuven and is a Clinical Investigator for the Flemish Fund for Scientific Research. His clinical expertise lies in acute cardiac care, interventional cardiology, pericardiology, as well as cardiac rehabilitation, while his current research focuses on antithrombotic therapies and the genomics of acute coronary syndromes. He is active in a variety of national and international boards and is involved in several clinical trials in cardiovascular disease as a steering or executive committee member. To date, Dr Sinnaeve has (co)authored 162 peer-reviewed papers and 26 book chapters.

About Idorsia

Idorsia Ltd is reaching out for more - We have more ideas, we see more opportunities and we want to help more patients. In order to achieve this, we will develop Idorsia into one of Europe's leading biopharmaceutical companies, with a strong scientific core.

Headquartered in Switzerland - a biotech-hub of Europe - Idorsia is specialized in the discovery and development of small molecules, to transform the horizon of therapeutic options. Idorsia has a broad portfolio of innovative drugs in the pipeline, an experienced team, a fully-functional research center, and a strong balance sheet – the ideal constellation to bringing R&D efforts to business success.

Idorsia was listed on the SIX Swiss Exchange (ticker symbol: IDIA) in June 2017 and has over 750 highly qualified specialists dedicated to realizing our ambitious targets.

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